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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,448	03/26/2001	H. Craig Dees	PHO-120	2388

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EXAMINER

HAQ, SHAFIQU

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/817,448

Applicant(s)

DEES ET AL.

Examiner

Shafiqul Haq

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 February 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 11-14, 16-18, 20-23, 25-31, 39, 40 and 46-50 is/are pending in the application.
- 4a) Of the above claim(s) 3, 16-18, 20-23, 25-28, 31 and 50 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 11-14, 29, 30, 39, 40 and 46-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 8/30/06
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/27/06 has been entered.

Response to Election/Restrictions

2. Applicants' election of invention of Group I, claims 1, 2, 11-14, 29-30, 39-40 and 46-49 and election of species (4,5,6,7-Tetrabromoerythrosin) filed 21 June 2006 in response to Office Action dated 02 June 2006 is acknowledged and entered. Because applicant did not distinctly and specifically present the reasons for traversal, the election has been treated as an election without traverse (MPEP § 818.03(a)). Accordingly, the restriction requirement is deemed proper and is made FINAL.
3. Accordingly, Claims 3, 16-18, 20-23, 25-28, 31 and 50 are withdrawn from further consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.
4. Claims 1-2, 11-14, 29-30, 39-40 and 46-49 are examined on merits.

Specification

5. The amendment filed June 8, 2005 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: "halogenated xanthenes of the present invention do not contain a radioisotope and are not radioactive."

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-2, 11-14, 29-30, 39-40 and 46-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not appear to provide literal or adequate descriptive support for the recitation of "said halogenated xanthene does not contain a radioisotope". This is a recitation of a negative limitation excluding radioisotope within the realm of the recited halogenated xanthene but the specification does not provide teaching or disclosure for the recitation of a negative limitation in the claims

excluding a radioisotope. Guidance for the specific exclusion of a radioisotope is not taught, the recitation of the negative limitation, "does not contain a radioisotope" is therefore not supported or disclosed in the instant specification.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 11-13, 29, 39-40 and 46-49 are rejected under 35U.S.C. 102(b) as being anticipated by Heitz et al. (US Patent 4,846,789).

Heitz et al. disclose halogenated xanthene dyes, which are administered to warm blooded animals and incorporated into infected tissue for activation by electromagnetic radiation (see Abstract and Figure 5). According to Heitz et al., the halogenated xanthene dyes may absorb radiation at wavelengths outside of the visible spectrum including near infrared, and near to far ultraviolet spectrum (see column 3, lines 40-44). Heitz et al. teach that fluorescein derivatives having one or more substituents in the 4, 5, 6, 7, 2', 4', 5', and 7' positions selected from the group consisting of F, Cl, Br, with xanthene dyes including erythrosin B, phloxin B, eosin, and Rose Bengal are especially important (see column 4, lines 12-31) and at least one of them anticipates the halogenated xanthene of present application. These halogenated xanthene dyes are incorporated into pharmaceutical delivery vehicles such as capsules or pellets for oral administration.

In as far as the recitation of "wherein said pharmaceutical composition increases the efficiency of conversion of applied ionizing radiation having an energy greater than approximately 1 keV into localized therapeutic effects against cancerous -----and animal tissue", a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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11. Claims 2, 14 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heitz et al. (US Patent 4,846,789).

Heitz et al. has been discussed supra.

Heitz et al. differ from the instant invention in failing to teach applying ionizing radiation having an energy less than approximately 1000 MeV (claim 14) or alternatively, greater than approximately 1 KeV. Heitz et al. also differ from the instant invention in failing to teach "0.001% to less than about 20% concentration".

However, different levels of ionizing radiation applied upon different halogenated xanthene dyes, and concentration levels of the halogenated xanthenes, constitute result effective variables which have been shown may be altered depending on how xanthene is used or the tissue being treated in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of *Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." *Id.* at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of *Boesch*, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the values recited in the claims 2, 14 and 30 are for any particular purpose or solve any stated problem and prior art has shown

that concentrations often vary according to use and purpose of the compound, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the ionizing radiation levels disclosed by the prior art by normal optimization procedures.

Response to Argument

12. Applicant's arguments and affidavit filed 2/27/06 have been fully considered, and are not persuasive to overcome the rejections of 8/25/05 under 35 USC 112, first paragraph, 35 USC 102 and 35 USC 103 as described in paragraphs 5-11 of this office action.

Applicant's arguments filed February 27, 2006 have been considered. Applicant argues that the recitation of "halogenated xanthene does not contain a radioisotope" is not new matter. Applicant specifically contends that the recitation is not new matter because discussion in the specification of the invention provides, 1) radiosensitizers as non-toxic in the absence of applied ionizing radiation; hence, they should not be radioactive and cannot contain any radioisotopes; 2) radiosensitizers that function to absorb light, not emit light; 3) molecular weights of the radiosensitizers as excluding radioisotopes as evidenced by examples in table 1; 4) molecular structures of the radiosensitizers as excluding radioisotopes; and 5) exclusion of radioisotopes in any of the chemical formula of the halogenated xanthenes.

In response, Applicant's argument is not persuasive because the specification lacks adequate descriptive support for the recitation of "said halogenated xanthene does not contain a radioisotope". This is a recitation of a negative limitation excluding radioisotope. Within the realm of the recited halogenated xanthene but the specification does not provide teaching or disclosure for the recitation of this negative limitation in the claims excluding a radioisotope. There is no guidance leading to the specific exclusion of a radioisotope in the specification. Table 1 shows "some example of halogenated xanthenes" and does not exclude radioisotopes. Since the limitations discussed lack antecedent basis in the specification, do not flow from the teaching of Applicant's disclosure and none of the originally filed claims recited the above limitations in question, they are considered to constitute new matter. See *In re ANDERSON*, 176 USPQ 331 (CCPA 1973). The mere absence of an element from a claimed structure is not consonant to requiring its exclusion from the structure.

Applicant argues prior art does not disclose highly halogenated xanthene as disclosed in present application. Applicant also contends that prior arts do not suggest use of halogenated xanthenes as radiosensitizer pharmaceutical composition for application with ionizing radiation. In response, Heitz et al. teach halogenated xanthene dyes which are fluorescein derivatives having one or more substituents in the 4, 5, 6, 7, 2', 4', 5', and 7' positions selected from the group consisting of F, Cl, Br, with xanthene dyes including erythrosin B, phloxin B, eosin, and Rose Bengal and at least one of them anticipates the halogenated xanthene of

present application. The compositions are administered to warm blooded animals and incorporated into infected tissue for activation by electromagnetic radiation. These halogenated xanthene dyes are incorporated into pharmaceutical delivery vehicles such as capsules or pellets for oral administration. These halogenated xanthenes encompass most if not all derivatives recited in claims 1, 29, 46, and 47; hence, Heitz deemed to anticipate the claimed invention.

In as far as the recitation of "wherein said pharmaceutical composition increases the efficiency of conversion of applied ionizing radiation having an energy greater than approximately 1 keV into localized therapeutic effects against cancerous -----
-----and animal tissue", a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963).

Conclusion

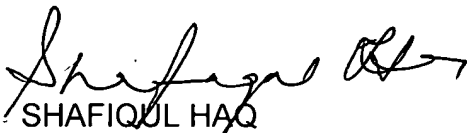
14. No claims are allowed.


15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiqul Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


SHAFIQUL HAQ
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